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10/566,466	01/31/2006	Ogari Pacheco	47050117PUS1	3749
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EXAMINER				
SCHLIENTZ, LEAH H				
ART UNIT		PAPER NUMBER		
1618				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary

Application No.

10/566,466

Applicant(s)

PACHECO ET AL.

Examiner

Leah Schlientz

Art Unit

1618

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 12 is/are allowed.
- 6) ☒ Claim(s) 1-11 and 13-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-850)
- Paper No(s)/Mail Date 1/31/06, 6/15/06, 7/31/06, 3/31/08
- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

In response to a telephone call from Applicant's Representative, Mark Nuell, regarding the Office action mailed 4/16/2009, the following corrective action is taken: the previous Office Action is vacated. Applicant's Representative directed the Examiner's attention to the amended Article 34 claims filed 1/31/2006. The previous Office Action mailed 4/16/2009 incorrectly addressed the original incorrect claim set. This Office Action addresses the amended claims 1-42. The period for reply set in said Office Action is restarted to begin with the mailing date of this letter.

Status of Claims

Claims 1-42 are pending and are examined herein on the merits for patentability.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 13-22, 24-31, 34-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to a stable pharmaceutical composition, characterized by comprising an amount of a fluoroether anesthetic compound selected from the group constituted of sevoflurane, desflurane, isoflurane, enflurane and methoxyflurane, and at least one stabilizer

employed in a concentration ranging from 0.001% to 5% in weight of the final composition. The phrase "and the like" in the claims renders the claims indefinite because it is unclear which further compounds are "like" those polyalcohols listed which are considered to be part of the claimed invention. See MPEP § 2173.05(b). The term "or like material" in the context of the limitation "coke, brick, or like material" was held to render the claim indefinite since it was not clear how the materials other than coke or brick had to resemble the two specified materials to satisfy the limitations of the claim. *Ex parte Caldwell*, 1906 C.D. 58 (Comm'r Pat. 1906). Likewise, the limitation that an alkyl substituted or unsubstituted aliphatic carbocyclic alcohol like menthol renders the claim indefinite. It is unclear how further compounds are "like" menthol in a way such that they are considered to be part of the claimed invention.

Claim 1-9, 13-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "alquil" does not appear to be a word commonly known in the English language, which may result from a translation discrepancy. The metes and bounds of the claim are unclear and the scope of the claim cannot be distinctly ascertained.

Claims 13-42 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are drawn to a method for stabilizing

sevoflurane characterized by "using at least one stabilizer agent, being the stabilizer agent a polyalcohol selected from the group constituted of propylene glycol, polyethylene glycol, etc...". However, the method fails to set forth any concrete steps regarding the actual practice of the method. The step of "using at least one stabilizer agent" does not constitute a concrete method step. Accordingly, the metes and bounds of the claims are unclear and the scope of the claims cannot be distinctly ascertained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13, 15 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Tobyn *et al.* (WO 03/018102).

Tobyn discloses that polyethylene glycol is a carrier for drugs including sevoflurane (claims 66, 79 and 100). It is noted that the recitation of the intended use of polyethylene glycol as a "stabilizing agent" has not been given patentable weight to distinguish over Tobyn because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since

Tobyn discloses compositions that are the same as those claimed, they would be capable of performing the intended use, as claimed.

Claims 13, 15, 17, 18 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Bieniarz *et al.* (US 6,271,422).

Bieniarz discloses the synthesis of sevofluorane from sevochlorane in PEG 400 solvent (see Figure 1 and column 6, lines 25-30), thus teaching a composition comprising sevoflurane in PEG 400. It is noted that the recitation of the intended use of polyethylene glycol as a "stabilizing agent" has not been given patentable weight to distinguish over Bieniarz because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since Bieniarz discloses compositions that are the same as those claimed, they would be capable of performing the intended use, as claimed.

Claims 1, 8, 23-29, 30-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang *et al.* (*Gaoxiang Yi Xue Ke Xue Zu Zhi*, 1990, 6(3), p. 127-30 (abstract)).

Yang discloses an inhalation anesthetic technique employed in rats. Polyethylene-glycol 400 (PEG 400) was first designed to combine with halothane to

produce a slow-releasing system of vaporized halothane. This design provided adequate anesthetic levels for treating with atracurium, a new neuromuscular blocking agent. Furthermore, isoflurane was also used in this study to examine this inhalation system for treating with atracurium. The efficient concentrations of inhaled anesthetics for adequate anesthesia when combining with PEG were 0.15% and 0.1% for halothane and isoflurane, respectively. This safe efficient state of anesthesia was maintained throughout the experimental course for treating atracurium, and might be used in clinical trials (abstract). It is noted that the recitation of the intended use of PEG 400 as a "stabilizing agent" has not been given patentable weight to distinguish over Yang because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since Yang discloses compositions that are the same as those claimed, they would be capable of performing the intended use, as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 4, 5, 8-11, 13, 14, 17-19, 22-29, 32-34, 37-39 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang *et al.* (*Gaoxiang Yi Xue Ke Xue Zu Zhi*, 1990, 6(3), p. 127-30 (abstract)), in view of Bieniarz *et al.* (US 5,990,176).

Yang discloses compositions comprising isoflurane and PEG 400 for providing slow-releasing anesthetic, as set forth above.

Yang does not specifically recite providing a sustained release formulation of sevoflurane using 0.1% PEG 400. It is for this reason that Bieniarz is joined.

Bieniarz discloses anesthetic compositions comprising a fluoroether compound and a physiologically acceptable Lewis acid inhibitor that exhibits improved stability and does not readily degrade in the presence of Lewis acid (abstract). Suitable fluoroether compounds include sevoflurane, enflurane, isoflurane, methoxyflurane and desflurane (column 4, lines 1-5). Preferably a lewis acid stabilizing agent is present in the amount of 0.015 to 0.14 percent (column 4, lines 31+). A container, such as a glass bottle may be washed with the lewis acid inhibitor and then filled with the fluoroether compound (column 5, lines 1-13).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute sevoflurane as a functionally equivalent fluoroether compound for isoflurane in the anesthetic compositions of Yang. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385, 1395-97 (2007) identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in *Graham*. One such rationale includes the simple substitution of one known element for another to obtain predictable results. The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. See MPEP 2143. In the instant case, the substituted components (isoflurane and sevoflurane) and their functions (anesthetic fluoroether compounds) were known in the art at the time of the instant invention, as shown by Bieniarz. One of ordinary skill in the art could have substituted one known anesthetic fluoroether for another, and the results of the substitution would have been predictable, that is preparation of a slow-releasing sevoflurane composition comprising PEG 400. Regarding claim 36, it would have been obvious to include 20 ppm water in the formulation because Bieniarz teaches that fluoroether compounds are stabilized from degradation products by inclusion of 0.015 to 0.14% water (column 4, lines 52-60). It is noted that the recitation of the intended use of PEG 400 as a "stabilizing agent" has not been given patentable weight to distinguish over Yang because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior

art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claims 1-3, 8-10, 13-16, 22-26, 32-36 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bieniarz *et al.* (US 5,990,176) in view of Brown *et al* (*Environmental Health Perspectives*, 1977, 21, p. 185-188).

Bieniarz discloses anesthetic compositions comprising a fluoroether compound and a physiologically acceptable Lewis acid inhibitor that exhibits improved stability and does not readily degrade in the presence of Lewis acid (abstract). Suitable fluoroether compounds include sevoflurane, enflurane, isoflurane, methoxyflurane and desflurane (column 4, lines 1-5). Preferably a lewis acid stabilizing agent is present in the amount of 0.015 to 0.14 percent (column 4, lines 31+). A container, such as a glass bottle may be washed with the lewis acid inhibitor and then filled with the fluoroether compound (column 5, lines 1-13).

Bieniarz does not specifically recite propylene glycol as a stabilizer. It is for this reason that Brown is joined.

Brown discloses that a debrominated derivative of halothane, an inhalation anesthetic, 1,1,1-trifluoro-2-chloroethane is unstable and should be prepared anearobically and stored in propylene glycol (abstract).

It would have been obvious to one of ordinary skill in the art to substitute propylene glycol as a functionally equivalent stabilizer to the stabilizing agents disclosed

in Bieniarz when the teaching of Bieniarz is taken in view of Brown. One would have been motivated do to so because both Bieniarz and Brown are drawn to fluorinated inhalation anesthetics, and because Brown teaches that propylene glycol can be used to stabilize unstable fluorinated inhalation anesthetics, such as 1,1,1-trifluoro-2-chloroethane. Bieniarz teaches that a lewis acid inhibitor useable in his formulations may be any compound that interacts with an empty orbital of a lewis acid, thereby blocking potential reaction sites of the acid. The hydroxyl moieties of propylene glycol would be capable of such activity, and furthermore Brown teaches propylene glycol to stabilize similar fluorinated anesthetics. It would have been obvious to use the claimed amount of propylene glycol because Bieniarz teaches 0.015 to 0.14 percent of stabilizer.

Conclusion

Claim 12 is free of the prior art. Claims 1-11 and 13-42 are rejected.

The following additional references is also made of record as being relevant to the instant invention, but is not relied upon for rejection: US 3,216,897 to Krantz.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS